

The Possible Synergistic Effects of Alcohol and Tobacco

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Abstract

It has now been well established that tobacco and alcohol use is positively correlated. The reasoning behind the concurrent use of both substances is an area of much research because both substances have the potential for dependence, are associated with health risks, and the theory that both these substances serve as a gateway for the use of stronger illicit drugs. Moreover, both nicotine, the addictive substance in tobacco, and alcohol, like other psychoactive substances, cause pleasure production and positive reinforcement via the mesolimbic dopamine system in the brain. Current research has suggested a possible neurobiological synergy of alcohol and nicotine and potential simultaneous binding on a certain type of receptor, nicotinic acetylcholine receptors, that may be present in the mesolimbic system. In addition, the combined use of nicotine and alcohol may have psychological antecedents that include personality traits like impulsivity and sensation- seeking.

Our study was designed to examine the relationship between alcohol and tobacco use through self-report measures. Participants from the spring 2007 UTEExperience 21st birthday study were given a Tobacco Use Index Questionnaire (TUI). TUI questions asked about normal tobacco use, how often tobacco products and alcohol are used together, and how many standard drinks are consumed before initiation of tobacco use. In addition, subjective one to ten scales were used to see if feelings of intoxication changed when tobacco products were used while drinking, whether feelings of intoxication were more enjoyable when tobacco products were used, and whether tobacco use was more enjoyable when drinking alcohol. Along with the TUI data, previously collected information on participants' values of sensation-seeking and impulsivity was analyzed to see if these values were associated with combined use.

Individuals were classified based on normal tobacco usage into categories. It was found that among all participants higher impulsivity was associated with increased percentage of time tobacco products were used while drinking alcohol. In addition, there were differences in percentage of time that alcohol and

tobacco products are used concurrently based on typical tobacco use. It was also found that individuals who only used tobacco products while drinking reported needing a higher number of standard drinks to initiate tobacco use than other categories of tobacco users. Lastly, tobacco users, regardless of normal frequency of tobacco use, did not report high levels of feelings of intoxication, changes in enjoyment of feelings of intoxication, or changes in enjoyment of tobacco use when tobacco products and alcohol were used together.

Due to the subjectivity of human based analysis, information from this study does not establish causality of neurobiological mechanisms, so more work done at the brain level needs to be done. Future areas of study include the characterization of the receptor types that bind both alcohol and nicotine in the brain as well as their location and effect on an individual's behavior. Moreover, other factors, including the psychological personality variables of sensation-seeking and impulsivity, need to be studied and combined with biological data to truly understand the interaction of alcohol and nicotine.

Introduction

The brain and spinal cord represent the largest part of our nervous system known as the central nervous system and, in conjunction with our peripheral nervous system, controls behavior. The functioning of our brain is based on electrical potentials that it uses to code and transmit information. These potentials can be modified by a variety of factors, the most important of which are the different types and levels of neurotransmitters and the receptors they specifically bind to. Neurotransmitters are chemical signals that modulate nervous system activity through the transfer, amplification, and/or inhibition of electrical potentials. This is done via charged particles (ions) that neurotransmitters cause to move into nervous system cells. This movement of ions affects the voltage potential of the target cell leading to a resultant change in its activity.

The Brain and Neurotransmitters

When at rest, cells of the nervous system (neurons) are relatively impermeable to charged particles but have regulated channels imbedded within their membranes that allow for the passage of specific ions. These channels are gated and open or close based on either potential (voltage-gated ion channels) or the presence of certain molecules (ligand-gated ion channels). These channels are specific for the type, charge, and size of ions they allow to pass in or out of the cell. If positive ions flow into a cell its potential increases and the passing of information is more likely; negative ions decrease voltage and have the opposite effect.

Ligand-gated channels are actually ion channels themselves. When a given molecule binds this type of receptor it initiates ion channel opening that causes either excitation (increase in voltage) or inhibition (decrease in voltage) into its target: the neuron that contains the receptor. This neuron can then transmit this excitation or inhibition information unto its next target. This is done via release of its own neurotransmitters that bind to the target cell's receptors and cause ion flow. Neurons are connected and ordered in pathways so that this information flow can be processed and ultimately result in the behavioral response of an individual.

Alcohol

Different stimuli can cause neurotransmitter release and can affect the nervous system and thus an individual's behavior in a variety of ways. Alcohol, a general term given to a class of organic compounds, is one such stimulus. The type of alcohol found in alcoholic beverages is ethanol, a flammable, strong smelling, and volatile chemical which affects many different neurotransmitters when consumed. This is the subtype of alcohol I deal with and will refer to whenever the term "alcohol" is used. This compound can be consumed both acutely and chronically, with some individuals developing dependence on the substance. Alcohol dependence has become a serious health problem: the American Psychiatric

Association reports that 19% of men and 8% of women have been diagnosed with alcohol dependence [6].

Alcohol and the Brain

Alcohol affects many different neurotransmitters in the brain depending on a variety of factors, some of which include- neuron location, receptor type, and whether alcohol is consumed acutely or chronically. Alcohol doesn't have its own endogenous receptors and thus alters brain function through a number of different receptor and neurotransmitter systems. The common mechanism is that alcohol binds to a ligand-gated receptor on a neuron. This binding opens the ion channel and changes the neuron's potential, usually by increasing the voltage. This increased potential causes the neuron to release neurotransmitters. The type of neurotransmitter released by this neuron is based on multiple factors, some of which include: the type of neuron, its location, and the type of receptor that alcohol initially bound to. Among the neurotransmitters affected are: Gamma-Aminobutyric Acid (GABA), Glutamate (GLU), Dopamine (DA), Norepinephrine (NE), and Serotonin (5HT).

Alcohol and Neurotransmitters: GABA, GLU, NE, and 5HT

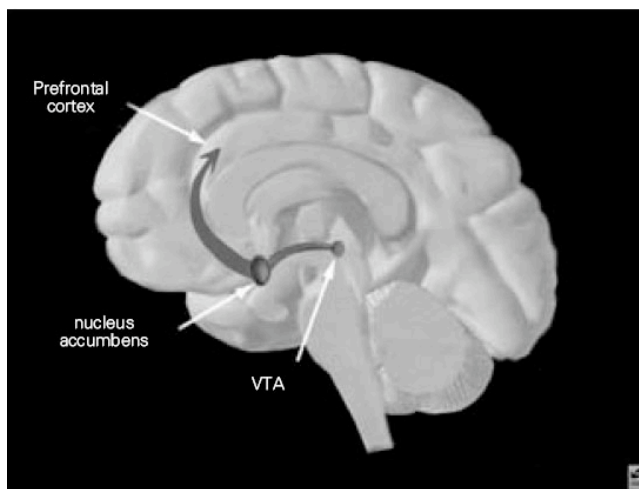
GABA, a neurotransmitter implicated in motor activity and sensory function, is thought to play an important role in the effects of alcohol through its ability to reduce anxiety. Through the increased response of certain GABA receptors, sedation and decreased muscle tone among other results can occur. Another neurotransmitter alcohol affects is GLU. Chronic exposure to alcohol, through modulation of glutamate receptors, may contribute to certain alcohol withdrawal symptoms, the development of tolerance, and neuronal cell death [8].

Alcohol also effects NE at low doses by enhancing its levels and causing arousal in an individual. Conversely, at high doses it decreases NE levels causing a sedative effect. In addition, alcohol increases levels of 5HT- neurotransmitter that aids in reducing information flow and increasing focus. This increase

in 5HT may be the mechanism by which alcohol causes intoxicated individuals to only focus on the most pertinent stimuli in their environment [8].

Alcohol and Neurotransmitters: Dopamine

Among the various neurotransmitters that alcohol affects, dopamine is the one of most interesting because of its involvement in the reinforcing effects of psychoactive substances. Dopamine is involved in four major pathways (mesolimbic, mesocortical, nigrostriatal, and tuberoinfundibular) that are classified based on the connections that are made between various brain areas. One such pathway is the mesolimbic system that links a region of the brain known as the ventral tegmental area (VTA) in the midbrain to the nucleus accumbens in the limbic system (see picture).



<http://www.greenfacts.org/en/psychoactive-drugs/images/figure-5-thumb.jpg>

When dopamine is released in this mesolimbic system, the behavioral result is that an individual experiences pleasure and reward. This dopamine release can be due to natural rewards like sex and food, or through drug consumption. Another closely related function of the mesolimbic dopamine system is the creation and maintenance of positive reinforcement. This describes a situation in which a specific behavior results in a positive consequence. This positive result increases the probability that an individual

will repeat the specific behavior that caused it. This is thought to influence drug self-administration [16]. For example, taking a drug increases the release of dopamine in the mesolimbic system that is translated to the individual as a pleasurable experience. The consequence, pleasurable feelings, is linked to the behavior that caused it, drug ingestion. Through reinforcement the drug taking behavior can become more likely to occur, and may lead to dependence. It has been shown that low doses of alcohol increase dopamine release in the nucleus accumbens and high doses increase dopamine in, among other areas, the VTA [8]. Thus, ethanol reinforcement, like that of many abused drugs, utilizes the mesolimbic DA pathways. Recently, researchers have shown this by injecting various drugs that bind and have similar effects as dopamine (agonists) or block the effects of endogenous dopamine (antagonists). Through microinjection of these drugs into both the nucleus accumbens and the VTA, the ethanol reinforcement response was altered. Thus, these data supports those of other researchers in showing that the mesolimbic pathway is involved in the mechanisms underlying ethanol reinforcement [15]. All of this evidence points to the fact that the reinforcing affects of alcohol, at least those resulting from acute administration, result from enhanced dopaminergic activity. Thus, alcohol's effects on brain neurotransmitter levels not only create the behavioral consequences, but also contribute to the reason's people consume this substance.

Alcohol and Psychological Factors

Alcohol's modulation of neurotransmitter levels is not the only factor involved in both the behavioral manifestations of alcohol consumption and reasons people chose to consume this substance, and possibly become dependent on it. Various psychological and environmental factors, such as expectancies, impulsivity, and sensation-seeking, among others, also come into play.

Alcohol and Psychological Factors: Expectancies

One such variable is a psychological concept known as expectancies. Alcohol expectancies are perceptions people have regarding alcohol and alcohol induced behaviors. They are preconceived notions that are shaped from past experiences with alcohol and factors such as peer group when drinking, social

setting, gender, situations you have seen while intoxicated, and the views of alcohol that an individual is socialized with. There are ways to test for a person's alcohol expectancies; for example the Comprehensive Effects of Alcohol questionnaire assesses both the positive and negative expected effects of alcohol as well as the subjective evaluation of those effects [5]. Evidence from various studies has shown that alcohol outcome expectancies play an important role in the creation and maintenance of differential alcohol consumption patterns in both adolescents and adults [7]. Thus, expectancies are one of many factors that determine both reasons for and effects of alcohol consumption.

Alcohol and Psychological Factors: Sensation-Seeking and Impulsivity

Impulsivity and sensation-seeking also play a role in alcohol consumption and alcohol manifested behaviors. Both are personality traits that can be measured based on self-report surveys. They are assumed to not change dramatically over time because they are based on inherent attributes of the individual. Impulsivity is a personality trait characterized by acting on impulse: behaviors are done without sufficient thought and there is a tendency to act with less forethought than other individuals. Impulsive individuals have rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions. There are several different forms of impulsivity, some of which have been linked to reduced nerve signal transmission mediated by the neurotransmitter serotonin. Cross-sectional studies have shown that impulsivity and novelty seeking have been associated with alcohol consumption and possibly dependence [12]. In addition, alcohol consumption has been shown to potentially increase impulsivity in individuals. Similarly, sensation-seeking is a tendency to seek exciting experiences. The neurobiological basis of this personality trait is still being elucidated but some researchers believe the neurotransmitters dopamine and serotonin may play a role. Studies have shown a correlation between high sensation-seeking ratings and the use of drugs, including alcohol [12]

Alcohol and Nicotine Use

The combination of aforementioned factors (modulation of neurotransmitter levels, environmental, personality, and psychological mediators) not only create alcohol's effect on the body but are also reasons why people consume this substance. The euphoric feelings associated with elevated dopamine levels, the anxiety reduction caused by GABA release, the expectancies an individual has about alcohol, the desire of some individuals toward risk-taking and novel stimuli, and still many other factors combine to create the antecedents that drive alcohol consumption. Moreover, these same reasons may underlie some individuals' transformation from acute alcohol consumption to dependence.

Some of these same variables are also the reasons behind the initial use, subsequent maintenance of use, and effects on the body of alcohol combined with other drugs. Nicotine is one such drug that is not only used with alcohol but has also been reported to create stronger subjective effects from concurrent use. The strong association between alcohol consumption and cigarette smoking, like alcohol combined with other drugs, is also likely to be attributable to multiple factors, including pharmacological actions common to both alcohol and nicotine [9].

Nicotine

Nicotine is the main addictive chemical in tobacco products and, like alcohol, affects different neurotransmitter levels in the central nervous system. A Center for Disease Control and Prevention study classified 25% of the adult U.S. population, about 48 million people, as current smokers (CDC, 1999). And approximately 30% of college-aged individuals use tobacco [10].

Nicotine and the Brain

This highly commonplace chemical exerts its brain altering effects by attaching to receptors on specific neurons and changing potential by affecting ion conductance. The consequences of this receptor binding

differ based on many factors including nicotine dose and length of use. Nicotine selectively binds to nicotinic acetylcholine receptors (nAChRs): ligand-gated ion channels that normally bind the chemical compound acetylcholine. Binding of nicotine to this receptor causes increased ion conductance, a subsequent change in the neuron's potential, and ultimately the release of neurotransmitters.

In general, nicotine at low doses increases attention, decreases anxiety, and improves concentration and memory. At high doses it can have a depressant effect on mood and arousal, though not as much as alcohol. Moreover, nicotine increases pleasure and thus can be reinforced and create dependence, similar to alcohol. The mechanism by which this occurs depends on the nAChRs located on dopamine neurons in the VTA (the brain region that has projections to the nucleus accumbens). Nicotine binds to these receptors and through excitatory potential changes causes dopamine release. Consequently, nicotine binding to nAChRs increases the activity of mesolimbic dopaminergic neurons in the brain's pleasure pathway. This not only gives the neurobiological reason for nicotine's ability to create pleasure but also provides a strong support for a mesolimbic mediated basis for nicotine reinforcement. Experiments have shown that if dopamine is decreased in the nucleus accumbens, thereby inhibiting the pleasure pathway and reinforcement, rats decrease their consumption of nicotine [18]. Moreover, blocking dopamine release in the nucleus accumbens with antagonists decreases the rewarding effects of nicotine, which is manifested in rats through reduced self-administration.

Alcohol and Tobacco Use

It has now been well established that tobacco and alcohol use is highly correlated: the amount of tobacco smoked is positively correlated with the amount of alcohol consumed [4]. Among alcoholics, 80%-95% are smokers as compared with 23% of the general population. Smoking is also highly correlated with drinking in nonalcoholic individuals, particularly those who are heavy drinkers [10]. The reasoning behind this co-occurrence is a current area of intense research because of its increasing prevalence, the potential for dependence that both substances have, the health risks associated with both alcohol and

nicotine, and the theory that both these substances serve as a gateway for the use of stronger illicit drugs. Moreover, elucidating the mechanisms underlying the concurrent use might allow for better treatment and prevention methods and, if a neurobiological basis for synergy is established, more targeted options that may be useful in treating both alcohol and nicotine dependence.

Alcohol and Nicotine: Psychological Factors

One potential reason for the initiation and maintenance of alcohol and nicotine use may be caused in part by personality traits of the user, such as impulsivity and sensation-seeking. In addition, expectancies might play a role. A recent study found that smokers were more likely to generate expectancies related to an increase in smoking while drinking [10]. As mentioned previously, expectancies may underlie the continuance of different alcohol related behaviors among individuals. Thus, preconceived notions related to smoking while drinking could play a role in the maintenance of this behavior. In addition, personality traits might also be a factor. Dependence on both alcohol and on nicotine has been found to be associated with high levels of impulsivity [9]. If an individual's innate impulsive behavior results in increased levels of alcohol or nicotine use, this may cause the concurrent use of these substances. Moreover, the increase in impulsive behavior caused by alcohol consumption may be a mechanism by which cigarette smoking increases when an individual is consuming alcohol.

Alcohol and Nicotine: Neurobiological Factors

On a neurobiological level, the mechanisms underlying concurrent use are twofold. When nicotine and alcohol are used together, humans describe a subjective enhancement that hints at a possible synergy at the neurobiological level. In addition, the maintained concurrent use of both substances may also be due to positive reinforcement that might stem from the enhanced pleasurable experience. In other words, if using both substances causes an increase in the feeling of pleasure for an individual, then the use of both substances will be reinforced; potentially a greater degree than the use of either substance alone.

The brain's mesolimbic system that controls pleasurable feelings and reinforcement is not only similar for both alcohol and nicotine but may also interact when both substances are used together. Treating laboratory animals with nicotine increases ethanol consumption and animals with high ethanol sensitivity have been shown to have high nicotine sensitivity as well [1]. In addition, nicotine antagonists - substances that block nicotine's effect on its receptors- injected into the VTA partially prevent alcohol's effects on the mesolimbic dopamine system [1]. Both of these findings suggest that alcohol might bind to the same receptors within the central nervous system that nicotine binds to. This also leads to the idea that nicotine and alcohol concurrence might involve a change in the aforementioned nAChRs. Current research is being done to determine whether the interaction of ethanol and nicotine is in fact mediated, at least partially, by nAChRs.

Nicotinic Acetylcholine Receptors: Activity and Location

Nicotinic acetylcholine receptors are found in various brain areas but one of particular interest is their possible location in the mesolimbic system, a pathway known to influence pleasure and reinforcement for both alcohol and nicotine. Some suggest that the increased dopamine levels in the VTA caused by alcohol might be mediated by the activation of mesolimbic nAChRs [3]. In other words, the very same receptors on dopamine neurons that bind nicotine endogenously, might also bind ethanol in the area of the brain that mediates pleasurable feelings and reinforcement. Moreover, if tobacco products are used during alcohol consumption then both of these chemicals might bind simultaneously to these nAChRs, increase ion flow through the receptor, and ultimately lead to increased dopamine release. This provides a brain location that might underlie and cause the synergy of these chemicals

The characterization of the nicotinic acetylcholine receptor subtypes and their distributions within the brain is difficult to determine. Moreover, the various subtypes of nAChRs each bind and interact with these drugs differently, making the mechanism of ethanol's interaction with these receptors and the interaction of both ethanol and nicotine hard to study. A 2003 study found that one of the subtypes of

nicotinic receptors, $\alpha 2\beta 4$, bound alcohols. They found two independent alcohol binding sites in these neuronal nAChRs: one excitatory, the other inhibitory. Short chain alcohols, including ethanol, bound preferentially to the excitatory site [2]. In other words, if ethanol bound to this excitatory site then ion flow through this receptor would be increased when nicotine was bound simultaneously. The resultant change in membrane potential due to this enhanced ion current would ultimately lead the neuron to release neurotransmitter. In this case, if ion flow is increased via alcohol binding to the excitatory site then neurotransmitter release may also be increased causing enhanced behavioral effects for the individual. This is a possible basis for the subjective enhancement that has been reported by human study participants when both nicotine and alcohol are consumed. Moreover, if these nAChRs that bind both alcohol and nicotine are found to be located in the mesolimbic dopamine system, then increased ion flow also causes increased neurotransmitter mediated effects in the brain area that mediates pleasure and reinforcement. Consequently, this could be the basis for the positive reinforcement of using both substances simultaneously.

Nicotinic Acetylcholine Receptors: Limitations

All of this research on the brain receptors that might mediate their synergistic effects is limited in their application to humans- the ultimate goal of all substance abuse research. For receptor characterization, it is still difficult to determine to which brain regions receptors are localized and whether these are the specific areas that are influenced when drug consumption occurs. In addition, rat studies, a common tool used to study drug consumption, are not always fully indicative of humans. This is because humans have many more variables involved that initiate and maintain the use of alcohol and nicotine as well as cause the resultant drug induced behaviors. Moreover, concepts like subjective enhancement and intoxication levels must be done by human self-report studies. More studies of this type need to be performed not just to test these results but also to provide more human information about the subjective effects and reinforcement of smoking while drinking.

My Research Aims: Alcohol and Nicotine

With the multitude of factors that moderate alcohol's effects on the brain, precede initial use, and underlie subsequent maintenance, there exists a very diverse field of research. The aforementioned psychological constructs of impulsivity and sensation-seeking as well as expectancies, and the neurobiological effects of neurotransmitter binding such as pleasure and positive reinforcement, are among many more factors involved.

With all of the possible areas to research, I chose to study the simultaneous use of nicotine and alcohol and the potential causes behind their concurrent use and subsequent maintenance for various reasons. For one, it is very applicable to my current peer group of college aged students. Recent evidence has found that the prevalence of smoking has increased over the past decade for this group [10]. Moreover, young adults are also likely to use alcohol and tobacco concurrently [10]. Thus, not only are there high levels of alcohol consumption in this group, but the concurrent consumption of alcohol with nicotine is a trend that continues to rise. Moreover, because of the potential ramifications of increasing the chance of using stronger illicit substances that these two so called "gateway drugs" cause, enhancing knowledge in this field might elucidate better prevention or treatment options.

My Research Aims: Self-Report Measures

Narrowing my area of research to the interaction between alcohol and nicotine still left a variety of topics to study. Because the final goal of all substance use and abuse research is its application to humans, and in this case college-aged individuals, I chose a psychology lab as my venue. Though neurobiological studies on receptor characterization, rat-self administration, and reinforcement further this area of research, they are limited in their application to humans; especially for concepts like subjective enhancement and intoxication levels. Moreover, self-report measures allow for larger sample sizes in smaller time periods than classic, animal-based neurobiological experiments. However, human self-report measures have several limitations that are caused for the most part by the amount of subjectivity involved.

This can be reduced with larger sample sizes and statistical analysis, but it still remains a factor that may skew results. In addition, results from such studies can often only establish correlation and not causation because the actual internal mechanisms of action are still unknown. Even with these limitations, the information gained from human self-report studies can shed light on this area of research, serve as a proxy for what is occurring at the neurobiological level, and provide possible direction for future research in both psychology and neurobiology.

My Research Aims: Questions I Aimed to Answer

Within the self-report parameters, I chose to study specific issues related to why individuals might consume alcohol and nicotine concurrently, as well as the outcome of combinatorial use. One question I wanted to answer is how often these substances are used in conjunction, and if this differs based on normal tobacco usage. This can be done by asking participants how often tobacco products are used while drinking alcohol and then comparing this information to their self-reported typical tobacco use. This can allow for specific analysis of those individuals who only use tobacco products while consuming alcohol (“typical tobacco use: only when drinking”). I believe there will be differences in percentages of time alcohol and tobacco are used concurrently based on self-reported typical tobacco use. It is easy to assume that regular tobacco users will continue to use tobacco even while consuming alcohol, and thus result in high percentages of the time alcohol and tobacco are used together. In addition, I believe that individuals who typically use tobacco only when drinking will report high percentages of time of using tobacco products while drinking. This is based on the idea that if the combined use of alcohol and nicotine is reinforced, then those individuals who only use tobacco products when they drink will almost always use tobacco products while drinking causing an increased self-reported percentage value. The science behind this theory is that when a consequence such as pleasure is linked to a behavior, in this case combined use, then that behavior will be reinforced. Moreover, if the use of both alcohol and nicotine does in fact act synergistically then this reinforcement should be shown in self-report measures and act as a proxy for possible neurobiological mechanisms. Of course, further research on the receptors in the mesolimbic

system that might potentially mediate these effects will need to be studied and ultimately help prove this idea.

The potential synergy of nicotine and alcohol and the idea that this might increase pleasure and thus initiate positive reinforcement can also be studied through self-report measures. Participants can be asked to compare their feelings of intoxication when tobacco products are consumed while drinking to when they are not. In addition, feelings of intoxication when using tobacco products as well as how much more enjoyable tobacco use is while drinking can also be found. These questions allow me to find out more about the potential enhanced subjective effects of both substances. I believe that participants who typically use tobacco, regardless of frequency, will report that combined use enhances pleasure, changes their feelings of intoxication toward higher more enjoyable levels, and makes tobacco use more enjoyable. This might be due to the fact that when alcohol binds nAChRs flow through this receptor is increased when nicotine is bound simultaneously. Thus, as previously mentioned, the combined use increases ion flow which may increase neurotransmitter mediated effects. If these nAChRs are in fact in the mesolimbic system then the increased behavioral effects would be pleasure and reinforcement, thus creating my hypothesized increase in self-reported enjoyment levels. However, this information from the human self-report studies can only serve as a proxy for what is actually occurring at the brain level. Thus, this is yet another area that will require more studies at the neurobiological level to characterize these receptors, their location, and the ultimate result of both nicotine and alcohol binding.

I also wanted to determine if there was a difference based on normal tobacco use on the number of standard drinks needed to initiate the consumption of tobacco products. I think individuals who only use tobacco products while consuming alcohol will require a larger number of standard drinks to initiate tobacco use. This can be done by asking individuals how many standard drinks they usually consume before starting to use tobacco products. A standard drink is defined as 12oz of beer, 5 oz of wine, or 1.5 oz of hard liquor either straight or in a mixed drink.

For other factors besides reward and positive reinforcement that might precede combinatorial use, I honed in on sensation-seeking and impulsivity, among all the other psychological factors, to study. Though many studies have linked these variables to just alcohol alone, there is less work on the combination of alcohol and nicotine. This would allow data gleaned to increase knowledge in this area. Through previous self-report data, I can analyze these psychological constructs and see if they affect combined use of alcohol and nicotine. My hypothesis is that these two factors would be positively associated with combinatorial use, thus, participants reporting higher levels of sensation-seeking and impulsivity will also report higher levels of using both nicotine and alcohol simultaneously.

Research Aims: Specific Hypotheses

1. Higher impulsivity and sensation-seeking will be associated with increased percentages of time that alcohol and tobacco products are used together.
2. There will be differences in percentage of time alcohol and tobacco products are used concurrently based on self-reported typical tobacco use. Specifically, individuals who only use tobacco products while drinking alcohol will report high percentages of time of concurrent use.
3. The number of standard drinks needed to initiate tobacco consumption will differ based on typical tobacco use. Specifically, individuals who only use tobacco when they drink will require more standard drinks to initiate tobacco use.
4. For tobacco users, regardless of normal frequency of tobacco use, feelings of pleasure, enjoyment from intoxication, and enjoyment from tobacco use will be high.

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Materials and Methods

Participants

Participants were selected from the larger, ongoing longitudinal study (“The UT Experience!”; UTE) based on their planned drinking during their 21st birthday celebration. Participants were 152 college-aged students who had regularly participated in UTE studies and had turned 21 the week prior to survey administration. The participants included 76 females and 76 males. 47.4% were Caucasian, 19.7% were Asian, 3.9% were Black/African-American, 2.6% had no ethnicity reported, and 0.7% were Native Hawaiian/Pacific Islander.

Participants were classified based on their responses to the question of “typical tobacco usage” found in the Tobacco Use Index section of the UTE 21st birthday self-report questionnaire packet. There were 105 participants who “never use” tobacco, 21 participants who reported tobacco use as “only when drinking”, 18 participants reported “rarely” using tobacco, and a total of 8 participants were in the “daily” and “weekly but not daily” tobacco use categories. The high number of participants who reported that they never use tobacco was removed from analyses in order to create more equivalent tobacco use categories.

The three resultant categories were thus Regular users, those who use tobacco products Only When Drinking, and those who Rarely use tobacco products.

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Procedure

Eligible individuals were contacted by telephone during the spring 2007 semester approximately one week before their 21st birthday to determine interest and screen out individuals who did not plan on consuming alcohol as part of their 21st birthday celebration. The phone screen assessed typical patterns of drinking and 21st birthday plans, including intentions to drink alcohol as part of their celebration.

Out of the 106 females and 106 males that were attempted to be recruited, the final 152 participants who were eligible and interested were invited to participate in a laboratory session within one week following their 21st birthday celebration.

During their time in the UTE laboratory, participants were asked to complete self-report questionnaires, which included the Tobacco Use Index (TUI; page 7 of measures). The 6-item TUI was developed for the current study and evaluates typical tobacco use, tobacco use while consuming alcohol, and changes in subjective response to alcohol and tobacco when used in conjunction.

To gauge personality traits, study data was used from past UTE surveys. Personality traits are thought to be stable and this information was collected from participants 3-months prior to starting college.

Measures

A 2003 study of subjective effects of smoking while drinking among college students (McKee, et al) was used as a reference for the questions included in the TUI. In this study participants were asked to rate how their smoking changed while drinking as well as what percentage of their smoking occurred while under the influence of alcohol [10]. The 6 question TUI given to participants in the UTE 21st birthday study, though based on McKee's study, was expanded and adapted beyond their self-report measures. See appendix for reference to TUI Questionnaire.

Question one asked how often the participant used tobacco products while drinking alcohol based on a 0 to 100 percentage of time scale. This is similar to the 2002 McKee study that used percentages but differs in that the TUI includes all tobacco products and not just cigarette smoking. In addition, question two asked participants to describe their typical tobacco usage based on a scale that included: never use, only when drinking, rarely, weekly but not daily, and daily. This allowed participants to be classified based on

their typical tobacco usage as well as to classify those individuals who only use tobacco when under the influence of alcohol. Question three, asked how many standard drinks the participant typically consumed before using tobacco products on a scale that included: 0, 1, 2, 3-5, 6-10, 11-13, 14-20, 20+, and N/A (never use tobacco).

The next set of questions asked participants to subjectively rate their feelings of intoxication and enjoyment. This was also based on the 2002 McKee study that asked individuals to rate whether their pleasure and desire for smoking or drinking changed as a result of concurrently using the other substance [10]. In our study, this possible pleasure change was also measured but through the use of three different questions. These three questions were expanded from the McKee study and included all tobacco products, not just cigarette smoking.

Question four of the TUI asked participants to compare their feelings of intoxication when consuming tobacco products while drinking to their feelings of intoxication when not using tobacco products. It was an incremental 1 to 10 scale ranging from 1 which was “no different” to 10 which was “extremely different”.

Question five asked individuals to rate how much more enjoyable their feelings of intoxication are when using tobacco products. For those who had never used tobacco products and alcohol together, they were asked to rate how much more enjoyable they thought the experience would be. This was based on a scale from 1 to 10 with 1 being “no more enjoyable” and 10 being “extremely more enjoyable”.

Question six asked participants to rate how much more enjoyable tobacco use is when drinking alcohol. For those who had never used tobacco products and alcohol together, they were asked to rate how much more enjoyable they thought the experience would be. The scale was again based from 1 to 10 with 1 being “no more enjoyable” and 10 being “extremely more enjoyable.”

Personality Characteristics (i.e., sensation-seeking and impulsivity) were assessed with the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ; Zuckerman, Kuhlman, Teta, Joireman, & Kraft, 1993).

Statistical Analysis

SPSS version 11.5 (SPSS Inc., Chicago IL) software was used to analyze data. Gender has been shown to differentially predict frequency and quantity of alcohol consumption with men typically reporting greater values for both [14]. Thus, gender was included in all analyses. Differences in indices of tobacco use and personality variables were assessed using seven separate 3 (Tobacco use group: Regular Users, Only When Drinking Users, Rare Users) x 2 (gender) factorial ANOVAs. As personality characteristics such as sensation-seeking and impulsivity have been shown to influence alcohol use and presumably other risky behaviors such as tobacco use [21], additional exploratory models included group x personality variable interaction terms. To assess specific differences, pair wise comparisons between groups were performed using independent sample *t*-tests. Finally, linear regression was used to examine the relation between personality characteristics and percent of time tobacco products were used while drinking. Final models included only statistically and marginally significant independent variables.

Results

Tobacco Use Categories

Examinations of typical tobacco use (TUI Q1) indicated that the majority of participants reported never using tobacco products (*n* = 105). Among participants who reported ever using tobacco, the majority reported using tobacco only when drinking (*n* = 21), followed by those who rarely use tobacco (*n* = 18), and lastly by regular tobacco users (*n* = 8).

Personality Characteristics and Tobacco Use in Conjunction with Alcohol Use

Related to hypothesis one, there was a marginally significant ($B = .111; p > .07$) association between higher sensation-seeking and increased percentage of time tobacco products were used in conjunction with alcohol. Higher impulsivity was found to be associated with increased percentage of time and was statistically significant ($B = .211; p > .05$). As shown in Table 2, there were no group differences in impulsivity ($p > .05$) or sensation-seeking ($p = .81$). There was also no interaction between group and sensation-seeking ($p > .05$) or impulsivity ($p > .05$) on percentage of time tobacco was used with alcohol.

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Comment: p values are rounded to two decimals unless they are $p < .001$

The tobacco use categories were compared for differences in percentage of time tobacco products were used while drinking, standard drinks consumed before using tobacco products, feelings of intoxication, enjoyment from intoxication, and enjoyment from tobacco use.

Percentage of Time Used Concurrently

Contrary to hypothesis two, those who only use tobacco when drinking alcohol had the lowest percentages of time of using alcohol and tobacco products together. Regular users had the highest percentage of time, followed by Rarely, and then Only When Drinking tobacco categories (see Table 1). There was a statistically significant difference ($p < .001$) between Regular and Rarely tobacco use categories for percentage of time alcohol and tobacco products were used together. This statistically significant difference was also shown between Regular and Only When Drinking tobacco usage categories ($p < .001$). There was no significant difference ($p > .05$) between Only When Drinking and Rarely tobacco usage categories.

Standard Drinks Needed to Initiate Tobacco Use

Supporting hypothesis three, there was a difference in standard drinks consumed before initiating tobacco use. Participants in the Only When Drinking tobacco use category needed the most number of standard drinks before using tobacco (see Table 1). A difference between the members of each tobacco usage

category on the mean number of standard drinks needed before using tobacco products was found to be statistically significant ($p < .05$; see Table 2). This difference between the means of the tobacco use categories was statistically significant between Only When Drinking and Regular tobacco categories ($p < .05$) and Only When Drinking and Rarely categories ($p < .01$). There were no statistically significant differences in number of standard drinks needed to initiate tobacco use between the Regular and Rarely tobacco categories ($p > .05$).

Feelings of Intoxication, Intoxication Enjoyment, and Tobacco Use Enjoyment

Contrary to hypothesis number four, there were no statistically significant differences between tobacco use categories on feelings of intoxication, enjoyment from intoxication, and enjoyment from tobacco use, Table 2.

Heather Brister

Comment: I would start each of the results paragraphs with contrary to or in support of hypothesis number XXX,.....

Conclusion

Participants were first divided into tobacco usage categories based on their self-reported regular tobacco use. Only those individuals who reported tobacco use, regardless of frequency, were included, as the large number of participants who reported that they never use tobacco would have skewed statistical analyses.

Alcohol and Nicotine: Sensation-Seeking and Impulsivity

Using participant information for personality measures as well as typical tobacco and alcohol use, it was found that higher values of impulsivity were associated with increased percentages of time that tobacco products were used while drinking. Sensation-seeking did not have a significant association with percentage of time alcohol and tobacco products were used concurrently for this participant sample.

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Comment: Be consistent in using past tense when reporting Results.

Impulsivity levels were compared across the tobacco use categories to see if there was any difference in impulsivity based on normal tobacco use but, no difference was found. Thus, being impulsive predicts an

increased percentage of time that alcohol and tobacco products are used in combination regardless of regular tobacco use. In addition, values of sensation-seeking were not found to differ based on typical tobacco use. It would be interesting to study this further and see what mechanisms might underlie impulsivity's connection to tobacco and alcohol usage. Perhaps, as past researchers thought, alcohol increases impulsivity levels that may underlie an individual's initiation of tobacco use. However, this is simply a conjecture that requires further study.

Alcohol and Nicotine: Percentage of Time Used Concurrently

Results revealed that regular tobacco users had the highest percentage of time of using both tobacco products and alcohol followed by those who rarely use, and lastly by those who only use tobacco while drinking. The fact that individuals who already use tobacco had higher percentages of time using tobacco while consuming alcohol was expected because these individuals are already regularly using tobacco. Moreover, regular users potentially already experienced a reinforcement and possible dependence to nicotine that may arise from regular tobacco use.

The hypothesis was not supported that those individuals who only used tobacco when drinking would show a higher percentage of time using tobacco while consuming alcohol.. This hypothesis was based on the idea that combined usage might provide greater reinforcement due to the pleasure produced when both drugs are used. Specifically, if concurrent binding to receptors in the mesolimbic system occurs, possibly even a greater reward and reinforcement response than with drug used alone. However, this hypothesis cannot be ruled out. More studies are needed with larger numbers of individuals who only use tobacco when drinking to study the percentage of time that this combined usage occurs. In addition, studies at the brain level analyzing receptor types and distributions within the mesolimbic system must also be done.

Alcohol and Nicotine: Standard Drinks Needed to Initiate Tobacco Use

Analysis proved that there was a difference based on self-reported typical tobacco use on number of standard drinks typically consumed before using tobacco products. In addition, this difference was only between those who only used tobacco when drinking and regular tobacco users, and those who only used tobacco when drinking and those who rarely used tobacco. Consequently, it appears that individuals who only use tobacco when they drink require a larger number of standard drinks before initiation of tobacco use. Perhaps in these individuals their levels of impulsivity increase while consuming alcohol which may initiate tobacco use. Or, that concurrent binding to receptors in the brain requires a threshold level of alcohol. Research in both psychology and biology on the interaction of standard drinks and the initiation of tobacco use while drinking could possibly shed light on this topic.

Alcohol and Nicotine: Feelings of Intoxication

The tobacco usage categories were used to compare participant's feelings of intoxication when consuming tobacco products and drinking to feelings of intoxication without the influence of tobacco products. It was hypothesized that all participants, regardless of normal tobacco use, were expected to report high values clustering around much more to extremely more enjoyable feelings of intoxication. The actual data proved that the average response for all groups was only "slightly different". In addition, differences in intoxication values based on normal tobacco use were examined. When compared across typical tobacco use categories, no difference was found in participant's feelings of intoxication. This lack of findings may be related to the wording of this particular question. When asked about their feelings of intoxication, there was no statement that allowed participants to rate their feelings even if they had never experienced concurrent tobacco and alcohol usage; this could be based on what a participant thinks will happen. This wording, that was included in the questions that followed about intoxication and tobacco use enjoyment, would have given all participants the ability to report a response. Consequently, many participants left this question blank further limiting the amount of data that could be analyzed. Future

studies could decrease this limitation and potentially increase participant numbers through a better worded question.

Alcohol and Nicotine: Intoxication Enjoyment and Tobacco Use Enjoyment

Participant ratings for how much more enjoyable feelings of intoxication would be when using tobacco compared to when not using tobacco products didn't reach the levels that were predicted, clustering around the "slightly more enjoyable" response. In addition, a similar but slightly higher average response was found for changes in enjoyment from tobacco use ranging between the responses "slightly more enjoyable" to "moderately more enjoyable." Further analysis proved that there was not a statistically significant difference between the tobacco use categories for ratings of enjoyment from tobacco use or enjoyment from intoxication. Consequently, normal tobacco usage doesn't seem to differentially predict enjoyment levels from either intoxication or tobacco use.

Increasing the number of individuals within each category and analyzing how they subjectively rate their enjoyment levels might provide more fruitful results. Further analysis with more participants should continue to make a distinction between how, if at all, feelings of intoxication change versus how, if at all, enjoyment from tobacco usage changes.

Alcohol and Nicotine: Overall Conclusions and Limitations

This study produced some interesting conclusions; however, many of the original hypotheses were not supported. The lack of conclusive results in some of the failed hypothesis may be attributable to limitations inherent in the experimental procedure.

For one, the large number of individuals who never use tobacco and were excluded from analysis made the data sample very small. The method used to classify participants based on self-reported typical tobacco use contributed to the small sample size. Research on tobacco and alcohol employs multiple

questions to determine tobacco status that include: number of tobacco products used in a lifetime, and amount of tobacco used within certain time frames. Using specific numbers for tobacco use allows for in-depth analysis and more accurate categorization. Moreover, having a reference number of tobacco usage for participants, like the classic “have you smoked more or less than a 100 cigarettes in your lifetime”, might shift some who have smoked occasionally or in the past but do not consider themselves tobacco users from the never use to rarely use category. The second possible reason for the small sample size was that participants were recruited to the study based on their involvement in the UTE 21st birthday study and not specifically for their normal alcohol and tobacco use. Recruitment of individuals who already use tobacco and selecting participants who represent specific tobacco use categories might yield stronger results.

Alcohol and Nicotine: Proposed Future Areas of Research

Much information is still unknown about the interaction between tobacco and alcohol. For one, self-report measures can only serve as proxies for neurobiological mechanisms. More research using rat self-administration of both nicotine and alcohol and possibly human brain imaging studies may help discover information at the biological level. In addition, characterizing nAChRs and their location in the brain as well as studying other neurotransmitter systems and receptor types for their possible role in mediating the interaction between alcohol and nicotine can provide useful data. Moreover, research should continue to try and understand the possible contributions of the brain’s reward and reinforcement mechanism in the combined use of alcohol and tobacco.

Research has shown that the factors that cause and maintain the individual usage of alcohol and nicotine is multifaceted, thus their combined use undoubtedly has many variables that come into play. Thus, other factors, including personality measures like impulsivity and sensation-seeking, require further study. Moreover, interdisciplinary approaches that combine information and data from both psychology and

biology need to occur in order for all the mechanisms behind the concurrent use of alcohol and tobacco products to be discovered.

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Appendix

TUI

1. How often do you use tobacco products <i>WHILE</i> drinking alcohol?	Percent of the Time									
	0%	10%	25%	40%	50%	60%	75%	90%	100%	
2. How would you describe your <i>TYPICAL</i> tobacco use?	Typical Tobacco Usage (please circle ONE statement)									
	Never Use		ONLY when drinking		Rarely		Weekly, but not daily		Daily	
3. How many standard drinks do you typically consume before using tobacco products?	Number of Drinks (please circle the number of drinks)									
	0	1	2	3-5	6-10	11-13	14-20	20+	N/A; never use tobacco	
4. Please compare your feelings of intoxication when you consume tobacco products while drinking to your feelings of intoxication when you do not use tobacco products										
1	2	3	4	5	6	7	8	9	10	
No Different		Slightly Different		Moderately Different		Much More Different		Very Different	Extremely Different	

5. Please rate how much more enjoyable your feelings of *INTOXICATION* are when using tobacco products. If you have never used tobacco products and alcohol together, please rate how much more enjoyable you think the experience would be.

1	2	3	4	5	6	7	8	9	10
No More Enjoyable		Slightly More Enjoyable		Moderately More Enjoyable		Much More Enjoyable		Very Much More Enjoyable	Extremely More Enjoyable

6. Please rate how much more enjoyable *TOBACCO USE* is when drinking alcohol. If you have never used tobacco products and alcohol together, please rate how much more enjoyable you think the experience would be.

1	2	3	4	5	6	7	8	9	10
No More Enjoyable		Slightly More Enjoyable		Moderately More Enjoyable		Much More Enjoyable		Very Much More Enjoyable	Extremely More Enjoyable

Data Tables

Table 1. Means for tobacco use categories and percent of time, standard drinks, feelings of intoxication, intoxication enjoyment, and tobacco use enjoyment.

Tobacco Use Categories			
Variable	Regular Users Mean (SD)	Only When Drinking Mean (SD)	Rarely Mean (SD)
Percentage of time tobacco used with alcohol (TUI Q1)	6.13 (2.64) ^a	1.81 (1.86) ^b	2.22 (1.96) ^b
Standard drinks before using tobacco products (TUI Q3)	2.13 (1.24) ^a	3.00 (0.75) ^b	2.00 (1.24) ^a
Feelings of intoxication (TUI Q4)	2.50 (2.00) ^a	3.00 (1.49) ^a	3.33 (2.20) ^a
Intoxication enjoyment (TUI Q5)	3.38 (2.72) ^a	3.23 (1.84) ^a	3.17 (2.57) ^a
Tobacco use enjoyment (TUI Q6)	5.88 (3.14) ^a	4.15 (3.28) ^a	3.50 (2.36) ^a

Note: Means with subscripts differ significantly at $p < .05$ by planned contrasts.

Table 2. Analysis of Variance for Tobacco Use Categories

Source	<i>F</i> (df)
Percentage of time tobacco used with alcohol (TUI Q1)	13.76 (2, 44)***
Standard drinks before using tobacco products (TUI Q3)	4.59 (2, 42)*
Feelings of intoxication (TUI Q4)	.533 (2, 43)
Intoxication enjoyment (TUI Q5)	.023 (2, 43)
Tobacco use enjoyment (TUI Q6)	1.83 (2, 43)
Impulsivity	.202 (2, 39)
Sensation-Seeking	.209 (2, 42)

* $P < 0.05$.** $P < 0.01$.*** $P < 0.001$.

